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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/235,875	01/22/99	MADISON L	MBX020

HM22/0326

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EXAMINER	
NELSON, A	
ART UNIT	**PAPER NUMBER**
1638	18
DATE MAILED:	03/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/235,875	MADISON ET AL.	
	Examiner	Art Unit	
	Amy Nelson	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. Claims 1-27, and 31-33 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is repeated for the reasons of record as set forth in the last Official action mailed 10/11/00. Applicant's arguments filed 2/20/01 have been fully considered but they are not persuasive.

Applicant asserts that Applicant is not claiming the genes *per se* as in the *Lilly* case law, but rather transgenic organisms comprising the genes (response, p. 7-8). Examiner responds that because the genes are required for production of the transgenic organisms, the same standard applies for the transgenic organisms as applies for the genes. Applicant has not described a representative number of the claimed genes, and hence Applicant has not provided an adequate written description of the genus of genes, and of transgenic organisms transformed therewith, in the instant specification.

Applicant further asserts that the genes required for the instant invention are known, and are present in the databases (response, p. 8). Applicant is invited to submit evidence of the availability of other genes before the time of filing of the instant application.

2. Claims 1-27, and 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to transgenic bacteria comprising a bacterial gene encoding β-ketoacyl-CoA reductase, a bacterial gene encoding β-ketothiolase, and an *A. caviae* gene encoding PHB polymerase that accepts 3-hydroxyhexanoyl CoA, and transgenic bacteria comprising a bacterial gene encoding PHB polymerase and an *A. caviae* gene encoding D-specific enoyl-CoA hydratase, as well as a method for producing polyhydroxyalkanoates comprising 3-hydroxyhexanoate by culturing said transgenic bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons of record as set forth in the last Official action mailed 10/11/00. Applicant's arguments filed 2/20/01 have been fully considered but they are not persuasive.

Applicant asserts that Examiner has not substantiated the rejections with cited art or with scientific reasoning. Specifically, Applicant asserts that Examiner has not provided a basis for the argument that only one sequence encodes the claimed enzymes, or that substrate specificity may be different among various species of a particular enzyme (response, p. 8). Examiner responds that the argument set forth by Examiner is that Applicant has not provided guidance for isolation of structurally and functionally genes reguired to produce the transgenic organisms encompassed by the broad scope of the claims. Specifically, Applicant has provided no guidance with respect to what hybridization/wash conditions or what PCR reaction conditions or what probe or primer sequences would allow specific isolation of additional functionally related genes. In the absence of

such guidance, undue trial and error experimentation would be required to screen through the vast number of cDNA and genomic clones from *A. caviae* or another bacterium, to identify those that are functionally related to the instantly disclosed genes and likewise encode a PHA polymerase that incorporates C_6 substrates or a D-specific enoyl-CoA hydratase.

Applicant asserts that it is well established in the art, that one can isolate genes from other organisms, once a sequence is isolated from a first organism. As an example, Applicant points to the isolation of PHB polymerase, beta-ketothiolase and acetoacetyl-CoA reductase genes from a variety of different bacteria. Applicant further notes that the specification teaches that a number of bacteria are able to utilize C5-C16 substrates to produce PHBH (response, p. 9). Examiner responds that the successful isolation of other genes as taught in the art does not enable isolation of the instantly claimed genes (and transgenic organisms comprising said genes). Genes differ in structural composition and degree of relatedness among organisms, and hence specific guidance is required for each gene/enzyme. It is not even clear that other bacteria produce the claimed genes (and encoded enzymes). Examiner can not find the cited text in the specification. However, even if other bacteria do utilize C5-C16 substrates, that still is not definitive evidence that other bacteria produce genes that encode a PHA polymerase that incorporates C_6 substrates or a D-specific enoyl-CoA hydratase.

Applicant also argues that bacterial genes have been expressed in plants since 1989, and Applicant cites specific U.S. Patents. In particular, Applicant asserts that previous publications have demonstrated the successful production of polymers in plants by introduction of bacterial

genes (response, p. 10). Examiner responds that the phenotypic effects of introduction of transgenes is unpredictable, as discussed in the last Official action, and as substantiated by the cited references. The specific phenotypic effects of the introduction of one transgene does not reduce the unpredictability of the phenotypic effects of another, functionally distinct transgene. Examiner does not question that bacterial genes can be successfully expressed in plants, but rather that the phenotypic effects of their expression can predicted. Moreover, as stated in the last Official action, it is not clear that the required substrates for the claimed genes/enzymes are present in plants, such that production of the claimed products could occur.

It is further reiterated that the enabled scope of the claimed invention is stated as above because it is not clear that introduction of either of the claimed transgenes alone is sufficient to confer the claimed phenotypes. It is well known in the art, for example, that introduction of all three of the genes, PHB polymerase, beta-ketothiolase and acetoacetyl-CoA reductase, is required to achieve production of PHAs in plants.

3. Claims 1-27, and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is in part repeated for the reasons of record as set forth in the last Official action mailed 10/11/00, and in part due to Applicant's amendments of the claims.

Claim 1 is indefinite because there is a lack of agreement between the preamble of the claim and the positive method step. In particular, the preamble of the claim recites "production of polyhydroxyalkanoate containing 3-hydroxyhexanoate," however the positive method step recites "production of polyhydroxybutyrate-polyhydroxyvalerate." Appropriate correction is required.

At Claim 1, line 8, the phrase, "under conditions suitable for production" is a meaningless phrase because Applicant has not specified the appropriate conditions. It is recommended that Applicant amend the claim to recite --wherein production of ... organism occurs--.

Claims 6-27 are improperly dependent on Claim 1. Applicant should amend the claims to clearly indicate how the single method step of Claim 1 (synthesizing) is modified. If additional method steps are intended then the claim language --further comprising-- should be inserted followed by the additional method step(s). If Applicant intends to further limit products recited within parent Claim 1, then the claim language --wherein said...-- should be recited. For example, Claim 6 is indefinite because Claim 1 recites "growing a transgenic organism ... having at least one bacterial transgene encoding an enzyme." The phrase "wherein the organism is genetically engineered" in Claim 6 reads as though Applicant intends an additional method step. It is recommended that Claim 6 be amended to recite --wherein the enzyme is...--. The other claims should be amended accordingly.

Claim 24 is improperly dependent on Claim 23. The claim should be amended to recite --wherein the enzymes are selected from the group...--.

At Claim 26, the phrase "the epimerizing enzymes" lacks proper antecedent basis in Claim 24. The phrase should be changed to --the enzymes--.

At Claim 27, "the organism that is genetically engineered" lacks proper antecedent basis.

At Claim 31, "transgenic bacterium or plant" should be changed to --transgenic bacterium or transgenic plant-- to clarify that the plant is also transgenic.

Claim 31 is dependent on canceled Claims 28-30.

Claims 18-27 are improperly dependent on Claim 1. Claim 1 is directed to a method of growing transgenic organisms having genes encoding specified enzymes. The claim does not recite a method step or organism which is "genetically engineered" and hence the recitation in Claim 18 and later claims of "further genetically engineered" does not make sense. Appropriate correction is required.

Claim Rejections - 35 USC § 102

4. Claims 1, 2, 5-11, 15, 31, and 32 remain rejected under 35 U.S.C. 102(a) as being anticipated by Fukui *et al.* (J. Bacteriol. 179: 4821-4830, 1997). This rejection is repeated for the reasons of record as set forth in the last Official action mailed 10/11/00. Applicant's arguments filed 2/20/01 have been fully considered but they are not persuasive.

Applicant asserts that Fuki does not specifically disclose incorporation of the introduced genes into the bacterial genome, as is recited in the instant claims (response, p. 11). Examiner responds that although the Fuki reference does not specifically recite that upon transformation of

the bacterial cells with the plasmid DNA, that the DNA becomes incorporated into the bacterial genome, it was well known in the art that bacterial transformation resulted in incorporation of the introduced DNA into the genome. Hence, bacterial cells were routinely grown for multiple generations in selection media just so that stably transformed cells would be selected. Because the process of stable bacterial transformation was so well known in the art, the use of the term "transformation" in the Fuki reference (*e.g.* p. 4821, right-hand column) was understood by one of skill in the art to mean stable transformation. Hence, it is submitted that the Fuki reference inherently discloses incorporation of the DNA into the bacterial genome.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Yolanda Vines, whose telephone number is (703) 305-2365.

AMY J. NELSON, PH.D
PRIMARY EXAMINER

Amy J. Nelson, Ph.D.
March 22, 2001